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REMARKS

Claims 1 – 19, 22, 24, 31, 35 and 48 are pending. Claims 20, 21, 23, 25 – 30, 32 – 34, 36 – 47, and 49 - 71 have been cancelled. Claims 10, 11, 14, 16, 22 have been amended. No new claims have been added. No new matter has been added by virtue of the amendments, support being found throughout the specification and claims as originally filed.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Objections

The Examiner argues that the oath or declaration is defective and a new oath or declaration in compliance with 37 CFR 1.67(a) is required. The Examiner argues that "the oath or declaration is defective because it does not identify the citizenship of each inventor. The citizenship of Yuntao Wu is absent." (Office Action, p.3).

Applicants submit a replacement declaration under separate cover in compliance with 37 CFR 1.67 (a). Applicants respectfully request withdrawal of the objection.

The Examiner has objected to the disclosure for minor informalities. The Examiner argues that "the specification contains blanks at pages 5, 6, 14, 15, and 16." (Office Action, p.2).

Applicants will provide ATCC accession numbers and date of deposits prior to allowance of the application. As set forth in In re Lundack (773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985)), the Court further held that the addition of information designating the depository, accession number, and deposit date of the deposited cell line in ATCC after the filing date did not violate the prohibition against new matter in 35 U.S.C. 132. In re Lundak 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985).

Accordingly, Applicants respectfully request withdrawal of the objection.

Claim Objections

The Examiner has objected to claims 10, 11, 14 and 15 for minor informalities. The Examiner argues that "claims 10 and 11 refer to figures." (Office Action, p.3). Applicants have amended claims 10 and 11 to no longer recite figures. The Examiner argues that claim 14 recites "improper Markush language." (Office Action, p.3). Applicants have amended the claims to recite proper Markush language.

Claim Rejections

35 U.S.C. §112, first paragraph, enablement

The Examiner has rejected claim 35 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement. The Examiner argues that "it is apparent that a specific host cell is required to practice the claimed invention (and) the host cell must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public (and) if it is not so obtainable or available, the requirements of 35 U.S.C 112, first paragraph, may be satisfied by a deposit of the host cell." (Office Action, p.3-4). Applicants disagree.

As pointed out above in In re Lundack, Applicant is not required to provide information designating the depository, accession number, and deposit date of the deposited cell line in ATCC at the time of filing. Accordingly, Applicant will provide the information prior to allowance.

Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §112, first paragraph, written description

The Examiner has rejected claim 22 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. The Examiner argues that "the claim is drawn to, inter alia, an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of: SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3, or a complement thereof, or a sequence which is at least about 60% identical to a nucleic acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3." (Office Action, p.5). The Examiner argues that "in the absence of sufficient recitation of distinguishing identifying characteristics, the

specification does not provide adequate written description of the claimed genus." (Office Action, p.6). Applicants disagree.

Claim 22 as amended recites an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; or a complement thereof, wherein the nucleic acid molecule comprises a GFP reporter gene, one or more splice donor sites, one or more splice acceptor sites and a HIV 5' and 3' LTR.

The instant specification sets forth in Figures 1 – 3 the expression constructs of SEQ ID NO: 1 – 3, respectively (see Figure 1 – 3 and the description on page 8). The instant specification sets forth in Figures 4 and 5 schematics of exemplary constructs containing one or more splice donor sites, one or more splice acceptor sites and a HIV 5' and 3' LTR. The instant specification teaches isolating and constructing the nucleic acid molecules of the invention (see, e.g. page 17, lines 8 – 12). The specification teaches complements of the sequences SEQ ID NO: 1, 2 or 3 of the invention, for example at page 17, lines 23 – 34 to page 18 line 5). The specification teaches how to determine percent identity at pages 18 – 19. The specification teaches that "the expressible sequence is only expressed when both Tat and Rev are present, (and) host cells containing the expression constructs of the invention can be infected with HIV and tested to identify compounds which can inhibit HIV infection and/or gene expression." (p.27, line 21 – 25).

Given the provided teaching, one of ordinary skill in the art could readily envisage a variety of nucleic acids that encode the isolated nucleic acid molecules of the invention. Methods of making nucleic acid sequences of any desired sequence are routine in the art. The claimed genus of nucleic acids is defined by the presence of the structures represented by SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3. Therefore, one skilled in the art would recognize that the applicant would have been in possession of a common distinguishing feature of members of the genus. The species shown in the specification's SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 is, therefore, representative of the species within the claimed genus.

Accordingly, Applicants respectfully request withdrawal of the objections.

35 U.S.C. §112, second paragraph

The Examiner has rejected claim 16 under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. The Examiner argues that "claim 16 recites the limitation 'the luciferase' in reference to claim 15 (but) there is insufficient antecedent basis for this limitation in the claim." (Office Action, p.7). Applicants respectfully traverse the rejection.

Claim 16 has been amended to recite proper antecedent basis. Accordingly, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §102(b)

The Examiner has rejected claims 1, 2, 13, 14, 16, 17, 18, 24 and 31 under 35 USC 102(b) as being anticipated by Saiga et al. (US Patent No. 6,090,783). Applicants respectfully traverse the rejection.

Claim 1 recites an isolated nucleic acid molecule comprising: a) a promoter, wherein the activity of the promoter is dependent on the presence of the human immunodeficiency virus (HIV) Tat protein; b) at least one splice donor site and at least one splice acceptor site; c) an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and d) a Rev Responsive Element (RRE) from the human immunodeficiency virus, wherein elements (a)-(d) are operably linked; and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof.

To anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure, § 2131.

The present invention is based, at least in part, on the discovery of novel DNA constructs which comprise an expressible sequence whose expression is dependent on the presence of both HIV Tat and Rev proteins. HIV Tat regulates transcription of the expressible sequence mRNA. Because the expressible sequence is contained; at least in part, within an intron; it is spliced out by the cellular splicing machinery unless Rev is present. The Rev Response Element (RRE) is necessary for Rev binding and activity. Accordingly, the expression constructs of the instant invention are capable of detecting

HIV infection and/or gene expression with both specificity and sensitivity. As taught in the specification at page 10:

> The HIV-dependent expression constructs comprise an expressible sequence expressed under the control of (i.e., operably linked to) an HIV-dependent promoter, for example, the HIV 5' LTR. The constructs further contain at least one splice acceptor-donor site pair and a Rev Responsive Element (RRE). When the HIV-dependent expression constructs are introduced into a cell, any mRNA transcribed from the expressible sequence will be spliced out if Rev is not present. However, when Rev is present (e.g., when the cell is infected with HIV), it will act through the RRE to prevent splicing of the expressible sequence. The expressible sequence can then be detected, either by detecting the mRNA or the encoded protein directly, or by detecting the activity of the encoded protein.

Applicants further point out Figures 4 and 5, which show at least one splice acceptor site is contained within the RRE.

The Saiga et al. reference does not teach or suggest all the limitations of the instant claims. In particular, the Saiga reference does not teach or suggest an isolated nucleic acid molecule comprising all the elements as taught in the instant claims, and in particular, an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and a Rev Responsive Element (RRE) from the human immunodeficiency virus, wherein elements (a)-(d) are operably linked; and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof.

The Saiga reference teaches DNA molecules and proteins associated with repression of gene expression and, in particular, a DNA molecule having a gene expression repressing function derived from human T-cell leukemia virus type I and a plasmid including the DNA molecule (see col. 1, lines 14 – 20). Figure 1, shown below, shows (a) the respective regions of the HTLV-1 genome, and (b) a plasmid constructed by incorporating the respective regions of the HTLV-1 genome between the region encoding the CAT gene and the bovine growth hormone polyA signal in a pRC/CMV-

CAT vector. Figure 9, also shown below, is a schematic diagram showing constituent units in a plasmid for gene therapy of HIV infectious diseases. In Figure 9, SA represents splice acceptor signal and SD represents splice donor signal.

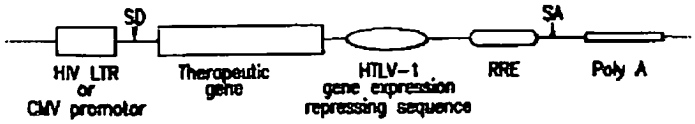

FIG.9

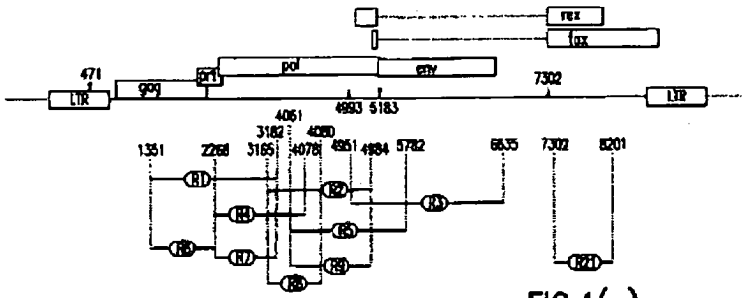

FIG.1(a)

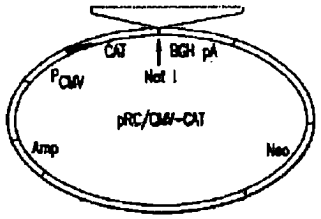

FIG.1(b)

Nowhere in the Figures or in the disclosure do Saiga et al. teach or suggest an isolated nucleic acid molecule comprising **all the elements** as taught in the instant claims, and in particular, an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and a Rev Responsive Element (RRE) from the human immunodeficiency virus, wherein elements (a)-(d) are

operably linked; and wherein the **at least one splice acceptor site is contained within the RRE**; or a complement thereof.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §103(a)

Claims 4 – 19 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Saiga et al. (US Patent No. 6,090,783, as above), as applied to claims 1, 2, 13, 14, 16, 17, 18, 24 and 31, above. Applicants respectfully traverse the rejection.

Instant claim 1 was set forth above. Claims 4 – 19 depend from claim 1.

As discussed above, the Saiga reference fails to teach or suggest all the elements of the instant invention. In particular, the Saiga reference does not teach or suggest an isolated nucleic acid molecule comprising **all the elements** as taught in the instant claims, and in particular, an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and a Rev Responsive Element (RRE) from the human immunodeficiency virus, wherein elements (a)-(d) are operably linked; and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof.

Therefore, in view of the teachings of the cited art, it would not have been predictable for one of skill in the art to substitute one reporter gene for another and result in the claimed invention.

Accordingly, Applicants request that the rejection be withdrawn.

Claims 1 – 18, 24 and 31 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Corbeau et al. (US Patent No. 6,323, 019), in view of Hope et al. (US Patent No. 6, 136, 597) and D'Costa (J of General Virology 2001, 82:425-434) and as evidenced by Saiga et al. Applicants respectfully traverse the rejection.

Instant claim 1 was set forth above.

The Corbeau et al. reference fails to teach or suggest all the elements of the instant invention. In particular, the Corbeau reference does not teach or suggest does not teach or suggest an isolated nucleic acid molecule comprising **all the elements** as

taught in the instant claims, and in particular, an expressible sequence which is not a wild-type HIV sequence, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and a Rev Responsive Element (RRE) from the human immunodeficiency virus, wherein elements (a)-(d) are operably linked; and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof.

Neither of the Hope nor the D'Costa references cure the defects of the Corbeau reference. Nowhere in either of the Hope or the D'Costa references is there teaching or suggestion of the an expressible sequence as instantly claimed, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and a Rev Responsive Element (RRE) from the human immunodeficiency virus, and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof. Therefore, the teachings of the cited art, when combined, do not result in the claimed invention.

The Examiner argues that "the choice and placement of splice donors and acceptors within a construct is well within the purview of one of ordinary skill in the art (and) it would have been obvious...to select HIV splice donors and acceptors...to incorporate into the claimed construct and the results would have been predictable." (Office Action, p.11). Applicants disagree. Applicants submit that the placement of splice donors is a novel feature of the instant invention. The present invention is based on the discovery of novel DNA constructs which comprise an expressible sequence whose expression is dependent on the presence of both HIV Tat and Rev proteins. Because the expressible sequence is contained; at least in part, within an intron; it is spliced out by the cellular splicing machinery unless Rev is present. The Rev Response Element (RRE) is necessary for Rev binding and activity. Accordingly, the expression constructs of the instant invention are capable of detecting HIV infection and/or gene expression with both specificity and sensitivity.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim 19 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over Saiga et al. or Corbeau et al. as applied to claim 1 above, and further in view of D'Costa et al. Applicants respectfully traverse the rejection.

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Claim 1 was set forth above. Claim 19 depends from claim 1 and recites that the nucleic acid molecule further comprises an internal ribosome entry site (IRES); or a complement thereof.

As discussed above, the Saiga reference and the Corbeau reference fail to teach or suggest all the elements of the instant invention.

The D'Costa reference does not cure the defects of either of the Saiga or the Corbeau references. Nowhere in the D'Costa reference is there teaching or suggestion of the an expressible sequence as instantly claimed, wherein at least part of the expressible sequence is located in an intron between the splice acceptor site and the splice donor site; and a Rev Responsive Element (RRE) from the human immunodeficiency virus, and wherein the at least one splice acceptor site is contained within the RRE; or a complement thereof. Therefore, the teachings of the cited art, when combined, do not result in the claimed invention.

Applicants respectfully request that the rejection be withdrawn.

CONCLUSIONS

In view of the above amendment, Applicant believes the pending application is in condition for allowance.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

By_____

Peter R. Corless
Registration No.: 33,860
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 439-4444
Attorneys/Agents For Applicant